

Indian krait venom and its therapeutic potential- A mini review

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ABSTRACT

Venoms, the secretions of venomous animals, are conventionally thought to be the source of toxic substances though the views about venoms in the recent era have been changed. Snake venom is a cocktail of multifunctional biomolecules that has evolved with the purpose of capturing prey as well as for defense. Due to their inherent high affinity and selectivity, many venom components are used as versatile biochemical tools or considered as prototypes of medicines. Bioactive components present in different snake venoms are mainly proteins and peptides either enzymatic or non-enzymatic which have tremendous therapeutic potential and are being used for the treatment of variety of diseases.

Kraits (*Bungarus* sp.) belong to Elapidae family and are widely distributed in East and South-East Asia. Krait venom possesses neurotoxins, membrane toxins, cardiotoxins, three finger toxins, metalloproteinases, cholinesterases, L-amino acid oxidases and serine proteases. The therapeutic potential of krait venom in pathophysiological conditions such as microbial/bacterial and parasitic infections, cancer, arthritis, inflammation, neuromuscular and blood coagulation disorder is discussed in this review. Further thorough research works are required to ascertain the therapeutic potential of krait venom in different diseases.

Key words: *Bungarus* sp., Therapeutic potential, Krait, Krait venom.

INTRODUCTION

Kraits are a group of highly venomous snakes found in parts of tropical Asia from Iran through the Indian subcontinent into the jungles of Borneo. There are 16 recognised species, with eight species from India and several more listed as subspecies. Kraits are nocturnal and typically have a non-aggressive behaviour. Yet, they are among the most medically important snakes, particularly in India, as they have the most toxic venom among terrestrial snakes found on the Indian subcontinent. Cobra and krait species belong to the family

Elapidae and are the most prevalent venomous snakes in India (Ghosh et al., 2016).

Venoms are a cocktail of bioactive molecules, and usually contain proteins and peptides as their main component (Ferraz et al., 2019; Suranse et al., 2018). They are used as a biological/chemical weapon in animals in addition to physical force for predatory purposes and sometimes as a defense mechanism when they are in danger. Animals that have venom include snakes, scorpions, spiders, cone snails and others. Despite the association of snake venom with pain

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and death, translational research has made good use of these venoms for basic science as well as the development of therapeutics inspired by snake venom toxins (Modahl et al., 2020; Koh and Kini, 2012).

Most venomous snakes are found in the Colubridae, Elapidae, Viperidae and Crotalidae families. The major snake bite mortalities are caused by four highly venomous snake species, *Naja naja*, *Daboia russelii*, *Echis carinatus* and *Bungarus caeruleus* or Indian krait which are commonly called as “Indian big four”. These four species of snakes, together, are responsible for over 50,000 reported annual deaths from snakebites in India. Kraits are one of the important members of Elapid family found in Indian subcontinent, North Asia, Southeast Asia, Sri Lanka, Myanmar. In eastern India, two types of kraits *Bungarus fasciatus* (the banded krait) and *Bungarus caeruleus* (the common krait) are common. The common name, krait, stems from the Hindi word “karait”, meaning black. The genus name, Bungarus, stems from the Telugu word, “Bungarum”, meaning gold. One would wonder how the two names for the same group can mean two distinct colours; the answer is that the names go back to the regions where the species were described. It turns out that the banded krait (*Bungarus fasciatus*) with its prominent gold bands was used to coin the genus name, while the word krait must have come from the Hindi heartland of central India where the predominantly black common Indian krait (*Bungarus caeruleus*) is encountered.

Envenoming due to krait (Genus: *Bungarus*) bites is a common, serious health issue in South and South-East Asia. Common krait (*Bungarus caeruleus*) is distributed throughout South Asia, and is responsible for large numbers of cases of severe neurotoxic envenoming each year (Valenta, 2010). It results in a descending flaccid paralysis progressing to life threatening respiratory paralysis unless mechanical ventilation is available (Alirol et al., Pe et al., 1997, 2010, Kularatne, 2002). Krait bites typically occur at night and are

not painful, so many patients do not notice the bite and continue sleeping (Kularatne, 2002; Bawaskar and Bawaskar, 2004; Warrell, 1983), which delays medical care.

“Numerous reports exist of the snake biting sleeping humans in the dead of night. The fact that the bite from this snake is not painful, unlike that of the spectacled cobra or Russell’s viper, adds to the mortality rate as people may not rush to get medical attention,” says Rom Whitaker, renowned herpetologist and co-founder of the Madras Crocodile Bank Trust. Krait venom is neurotoxic and often causes paralysis of muscles, leading to respiratory failure.

Globally snake envenoming is a major cause of morbidity and mortality in the rural tropics (Kasturiratne et al., 2008). Neurotoxicity causing paralysis is one of the major clinical syndromes of snake envenoming, and occurs mainly with Elapids. Despite the magnitude of the health impact of neurotoxic snake envenoming, it continues to be associated with several unresolved issues of clinical importance (Ranawaka et al., 2013). Several reports regarding the therapeutic potential of venom of different elapid snakes and their purified toxins have been found (Mukherjee et al., 2011).

Therapeutic potential of Krait venom:

Therapeutically krait venom had been reported for treatment in different diseased condition. Bungarotoxin isolated from *B. multicinctus*, a member of krait family found in Thailand, Myanmar has been reported to be used in homeopathic treatment of cholinergic disease such as Alzheimer’s due to its ability to inhibit choline uptake ([http:// www.scribd.com/doc/29470339/VENOMS](http://www.scribd.com/doc/29470339/VENOMS))

Krait venom is used in treatment of myasthenia gravis (Coulter, 1994). Usage of krait venom to treat different diseases was mentioned in homeopathy and Chinese medicine. Very few reports regarding therapeutic potential of two types of Indian krait *B. fasciatus* and *B. caeruleus* venom have been available so far.



Fig 1: *Bungarus caeruleus* in India (Source: https://www.inaturalist.org/taxa/96224-Bungarus-caeruleus/browse_photos)

Source: www.iucn.org.

An antivenom antibody was raised in chicken against *B. caeruleus* and *Naja naja* venom was experimentally used *in vivo* and *in vitro* experiments to neutralize venom induced toxicities. This specific antibody (IgY) had molecular weight of 180 kDa and able to neutralize venom induced lethal effect on Swiss albino mice, phospholipase A₂ activity, paw edema activity. In procoagulant neutralizing experiment with IgY, clot formation was not observed. Cathelicidin-BF a cathelicidin like antimicrobial peptide was purified from *B. fasciatus* through gel filtration and RP-HPLC was tested against forty (40) microorganism strains. Cathelicidin-BF was mostly potent against Gram negative bacteria like *E. coli*, clinically isolated strain *Salmonella typhi* and also effective against fungi like *C. albicans*, saprophytic fungus (*A. terreus*). Clinically used antibiotics like ampicillin, benzylpenicillin possessed no effect on any of these strains (Wang et al., 2008). In another study it had been found that Cathelicidin-BF killed *Propionibacterium acnes*, *Staphylococcus epidermidis* responsible pathogen for acne vulgaris. It inhibited *P. acne* induced O₂^{•-} production, pro inflammatory cytokines production *in vitro*. In mice model *P. acne* induced ear swelling, granulomatus inflammation was successfully restored after



Fig 2: *Bungarus fasciatus* (Source: <https://www.indianreptiles.org/sp/420/Bungarus-fasciatus>)

Cathelicidin-BF treatment (Wang et al., 2011). Therefore, Cathelicidin-BF has potency for therapeutic use against resistive strains of different microorganisms as well as against acne vulgaris. A L-amino acid oxidase from *B. fasciatus* purified through chromatographic procedure having molecular weight of 70 kDa, showed cytotoxic effect on A549 (adenocarcinomic human alveolar basal epithelial cells) cell line after 12 hrs treatment (Wei et al., 2009). A neurotoxin purified from *B. caeruleus* caused blockade in isolated frog rectus abdominis muscle preparation and might be used as a therapeutic agent in the treatment of neuromuscular disorder (Mirajkar et al., 2006).

A novel group IAs PLA₂ named BFPA isolated from *B. fasciatus* snake venom showed potent bactericidal activity against both Gram positive (*Staphylococcus aureus*) and Gram negative (*Escherichia coli*) bacteria. This BFPA also increased Ca²⁺ induced clotting time of platelet poor plasma i.e showed anticoagulant activity (Xu et al., 2007). This can provide a drug development evidence against thrombosis and related cardiovascular diseases.

An anti PLA₂ rabbit antiserum was produced against a toxic PLA₂ (BF-38) of *B. fasciatus* venom after hyperimmunization of rabbit. This

anti PLA₂ rabbit antiserum along with 2-hydroxy-4-methoxy benzoic acid (a herbal origin venom antagonist) neutralize venom induced toxicities like PLA₂ activity, paw edema, plasma recalcification and cardiotoxicity which is comparable with commercial polyvalent anti snake venom antisera. So, in case of banded krait envenomation the combination therapy of anti PLA₂ rabbit antiserum with herbal antagonist might produce better snakebite management in rural areas (Gomes et al., 2012). The krait venoms/toxins may also help in developing newer antidotes for snakebite victims.

CONCLUSION

Although limited scientific reports are available on Indian krait venoms and their purified toxins, they do imply towards therapeutic potentials against neurological disorders, bacterial, parasitic infections, cancer and several other diseases. Further detailed study with krait venoms may decipher not only new intimations towards developing novel life saving drugs and diagnostic reagents in the near future but also elucidating as a biological tool.

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